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STRUCTURE FILE UPDATES: 20 MAR 2008 HIGHEST RN 1009361-91-4 DICTIONARY FILE UPDATES: 20 MAR 2008 HIGHEST RN 1009361-91-4

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http://www.cas.org/support/stngen/stndoc/properties.html

 ${\tt Uploading \ C:\ Program \ Files \ Stnexp\ Queries \ \ 10561212.str}$

L1 STRUCTURE UPLOADED

=> d 11

L1 HAS NO ANSWERS

Structure attributes must be viewed using STN Express query preparation.

=> s 11 exact
SAMPLE SEARCH INITIATED 16:39:31 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 1 TO ITERATE

100.0% PROCESSED 1 ITERATIONS 0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE** BATCH **COMPLETE**

80 1 TO PROJECTED ITERATIONS: PROJECTED ANSWERS: 0 TO 0

L2 0 SEA EXA SAM L1

=> s 11 sss sam

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100.0% PROCESSED 1 ITERATIONS 0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

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0 SEA SSS SAM L1

=> file caplus

SINCE FILE TOTAL SESSION 1.13 COST IN U.S. DOLLARS

FULL ESTIMATED COST 0.92 1.13

FILE 'CAPLUS' ENTERED AT 16:40:12 ON 21 MAR 2008 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

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FILE COVERS 1907 - 21 Mar 2008 VOL 148 ISS 13 FILE LAST UPDATED: 20 Mar 2008 (20080320/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

=> s ?benzazepine

L43243 ?BENZAZEPINE

=> s 14 and triazolo

7589 TRIAZOLO

T.5 29 L4 AND TRIAZOLO

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                 (CELLULOSE OR CELLULOSES)
L6
             2 L5 AND CELLULOSE
=> dis 16 1-2 bib abs
     ANSWER 1 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
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ΑN
DN
     142:62766
ΤI
     Product of coprecipitation of sparingly soluble substance and
     water-soluble polymer and process for producing the same
     Ishikura, Toyoaki; Udagawa, Chikako; Misaka, Masato; Suemune, Kenji;
ΙN
     Kitahara, Shinichi; Ono, Kiyoko; Koyanagi, Akihiro
    Meiji Seika Kaisha, Ltd., Japan
PA
SO
     PCT Int. Appl., 31 pp.
     CODEN: PIXXD2
DT
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LA
    Japanese
FAN.CNT 2
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                       KIND
                                DATE
                                          APPLICATION NO.
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                         Α1
                               20070719
                                           US 2005-561212
                                                                   20051219
PRAI JP 2003-175646
                         Α
                                20030620
     WO 2004-JP8727
                                20040621
AB
     Disclosed is a product of the copptn. of 2-(1-isopropoxy-carbonyloxy-2-
     methylpropyl)-7,8-dimethoxy-4(5H),10-dioxo-2H-1,2,3-triazolo
     [4,5-c][1]benzoazepine (I) and a water-soluble polymer. The copptn. product
     is excellent in solubility and absorbability. Crystalline I and Me
     cellulose were dissolved in DMSO. The mixture was dropped into an
     aqueous solution containing Me cellulose to give ppts., which showed a
     solubility 16.8 \mu g/mL, as compared to 0.8 \mu g/mL for crystalline I.
              THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT 15
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
     ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
L6
     2003:532667 CAPLUS
ΑN
     139:90493
DN
ΤI
     Amorphous substance of tricyclic triazolobenzazepine derivative
ΙN
     Ishikura, Toyoaki; Ishizawa, Takayuki; Suemune, Kenji; Ishiwata, Mayumi;
     Udagawa, Chikako
PΑ
    Meiji Seika Kaisha, Ltd., Japan
SO
    PCT Int. Appl., 25 pp.
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Patent
LA
     Japanese
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     WO 2003055886 A1 20001
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                         A1 20030710 WO 2002-JP13558 20021225
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             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
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     US 2005130955
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                              20070612
                         В2
     US 7229985
                             20011226
     JP 2001-393016 A
WO 2002-JP13558 W
PRAI JP 2001-393016
                                20021225
AΒ
     Disclosed are amorphous 2-(1-isopropoxycarbonyloxy-2-methylpropyl)-7,8-
     dimethoxy-4(5H), 10-dioxo-2H-1, 2, 3-triazolo[4, 5-c][1]
     benzazepine (I), which is improved in absorbability and solubility; and
     a medicinal composition containing the compound Also provided are processes
for
     producing amorphous compound I and for producing a medicinal composition
containing
     the compound An amorphous compound I was dissolved in methylene chloride, and
     mixed with Me cellulose (Metolose SM15) and methanol. The mixture
     was then spray dried to obtain an amorphous powder of the present
     invention.
RE.CNT 11
              THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
=> s 15 and coprecip?
          6863 COPRECIP?
          2591 COPPT
          1482 COPPTS
          3609 COPPT
                 (COPPT OR COPPTS)
          6440 COPPTD
          1034 COPPTG
         17317 COPPTN
            61 COPPTNS
         17339 COPPTN
                 (COPPTN OR COPPTNS)
         25841 COPRECIP?
                 (COPRECIP? OR COPPT OR COPPTD OR COPPTG OR COPPTN)
L7
             1 L5 AND COPRECIP?
=> dis 17 bib abs
    ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN
T.7
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CODEN: PIXXD2

DT

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DN
     142:62766
     Product of coprecipitation of sparingly soluble substance and
ΤI
     water-soluble polymer and process for producing the same
     Ishikura, Toyoaki; Udagawa, Chikako; Misaka, Masato; Suemune, Kenji;
IN
     Kitahara, Shinichi; Ono, Kiyoko; Koyanagi, Akihiro
PA
     Meiji Seika Kaisha, Ltd., Japan
SO
     PCT Int. Appl., 31 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     Japanese
FAN.CNT 2
     PATENT NO.
                          KIND
                                   DATE
                                               APPLICATION NO.
                                                                         DATE
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PΙ
     WO 2004113451
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,

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EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,

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                                              US 2005-561212
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PRAI JP 2003-175646
                            Α
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     WO 2004-JP8727
                            W
                                   20040621
     Disclosed is a product of the copptn. of 2-(1-isopropoxy-
AΒ
     carbonyloxy-2-methylpropyl)-7,8-dimethoxy-4(5H),10-dioxo-2H-1,2,3-
     triazolo[4,5-c][1]benzoazepine (I) and a water-soluble polymer. The
     copptn. product is excellent in solubility and absorbability. Crystalline I
     and Me cellulose were dissolved in DMSO. The mixture was dropped into an
     aqueous solution containing Me cellulose to give ppts., which showed a
solubility 16.8
     \mug/mL, as compared to 0.8 \mug/mL for crystalline I.
RE.CNT 15
               THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
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=> s 15 and allerg?
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              3 L5 AND ALLERG?
1.8
=> dis 18 1-3 bib abs
L8
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     2004:1154779 CAPLUS
ΑN
DN
     142:62766
     Product of coprecipitation of sparingly soluble substance and
ΤI
     water-soluble polymer and process for producing the same
     Ishikura, Toyoaki; Udagawa, Chikako; Misaka, Masato; Suemune, Kenji;
ΙN
     Kitahara, Shinichi; Ono, Kiyoko; Koyanagi, Akihiro
PΑ
     Meiji Seika Kaisha, Ltd., Japan
     PCT Int. Appl., 31 pp.
SO
     CODEN: PIXXD2
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DT
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2004:1154779 CAPLUS

ΑN

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LA
    Japanese
FAN.CNT 2
                       KIND DATE APPLICATION NO. DATE
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PRAI JP 2003-175646
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                               20030620
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     Disclosed is a product of the copptn. of 2-(1-isopropoxy-carbonyloxy-2-
AΒ
     methylpropyl)-7,8-dimethoxy-4(5H),10-dioxo-2H-1,2,3-triazolo
     [4,5-c][1]benzoazepine (I) and a water-soluble polymer. The copptn. product
     is excellent in solubility and absorbability. Crystalline I and Me cellulose
were
    dissolved in DMSO. The mixture was dropped into an aqueous solution
containing Me
     cellulose to give ppts., which showed a solubility 16.8 \mug/mL, as compared
     to 0.8 \mug/mL for crystalline I.
RE.CNT 15
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     ANSWER 2 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
ΑN
     2004:1154716 CAPLUS
DN
     142:100324
     Tricyclic triazolobenzazepine derivative produced as novel
ΤI
     crystalline substance
     Kitahara, Shinichi; Yamaguchi, Toshihiro
ΙN
PA
     Meiji Seika Kaisha, Ltd., Japan
     PCT Int. Appl., 21 pp.
SO
     CODEN: PIXXD2
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     WO 2004-JP8729
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     Crystalline 2-(1-isopropoxycarbonyloxy-2-methylpropyl)-7,8-dimethoxy-4(5-H),10-
AB
     dioxo-2H-1, 2, 3-triazolo[4, 5-c][1]benzazepine (I) (X
     ray crystallog. data given) is claimed. The crystals of I of this
     invention have high solubility and bioavailability. Crystallization of I from
     water gave \beta type crystals of I. I is an antiallergic agent.
              THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT 13
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     2003:532666 CAPLUS
ΑN
     139:95490
DN
     Crystalline tricyclic triazolobenzazepine derivative
ΤI
     Kitahara, Shin-Ichi; Furukawa, Hanae; Yamaguchi, Toshihiro; Miyamoto,
IN
     Sachiko; Okada, Yumiko
PA
     Meiji Seika Kaisha, Ltd., Japan
SO
     PCT Int. Appl., 17 pp.
     CODEN: PIXXD2
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     Patent
    Japanese
LA
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PRAI JP 2001-393016
                               20011226
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     WO 2002-JP13557
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     Crystalline 2-(1-isopropoxycarbonyloxy-2-methylpropyl)-7,8-dimethoxy-4(5-H),10-
AB
     dioxo-2H-1, 2, 3-triazolo[4, 5-c][1] benzazepine (I) (X
     ray crystallog. data given) is claimed. I is an antiallergic agent.
             THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
=> s 15 and polymer
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=> s 15 and polymer
1184051 POLYMER
943758 POLYMERS
1583621 POLYMER
(POLYMER OR POLYMERS)
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=> dis 19 1-2 bib abs
      ANSWER 1 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
L9
      2004:1154779 CAPLUS
ΑN
DN
      142:62766
ΤI
      Product of coprecipitation of sparingly soluble substance and
      water-soluble polymer and process for producing the same
IN
      Ishikura, Toyoaki; Udaqawa, Chikako; Misaka, Masato; Suemune, Kenji;
      Kitahara, Shinichi; Ono, Kiyoko; Koyanagi, Akihiro
      Meiji Seika Kaisha, Ltd., Japan
PA
SO
      PCT Int. Appl., 31 pp.
      CODEN: PIXXD2
DT
      Patent
      Japanese
LA
FAN.CNT 2
      PATENT NO.
                               KIND
                                                       APPLICATION NO.
                                         DATE
                                                                                      DATE
                                ____
      WO 2004113451
                                         20041229
                                                       WO 2004-JP8727
                                                                                       20040621
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           W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE,
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      US 2007167402
                                                       US 2005-561212
                                 Α1
                                         20070719
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PRAI JP 2003-175646
                                 Α
                                          20030620
      WO 2004-JP8727
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                                          20040621
AΒ
      Disclosed is a product of the copptn. of 2-(1-isopropoxy-carbonyloxy-2-
      methylpropyl)-7,8-dimethoxy-4(5H),10-dioxo-2H-1,2,3-triazolo
      [4,5-c][1]benzoazepine (I) and a water-soluble polymer. The
      copptn. product is excellent in solubility and absorbability. Crystalline I
      cellulose were dissolved in DMSO. The mixture was dropped into an aqueous
solution
      containing Me cellulose to give ppts., which showed a solubility 16.8 µg/mL,
      compared to 0.8 \mug/mL for crystalline I.
                  THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT 15
                  ALL CITATIONS AVAILABLE IN THE RE FORMAT
      ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
L9
ΑN
      2003:532667 CAPLUS
DN
      139:90493
ΤI
      Amorphous substance of tricyclic triazolobenzazepine derivative
      Ishikura, Toyoaki; Ishizawa, Takayuki; Suemune, Kenji; Ishiwata, Mayumi;
ΙN
      Udagawa, Chikako
      Meiji Seika Kaisha, Ltd., Japan
PA
SO
      PCT Int. Appl., 25 pp.
      CODEN: PIXXD2
DT
      Patent
LA
      Japanese
FAN.CNT 2
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            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
            PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
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A1 20041013 EP 2002-790871
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                     A 20050518 CN 2002-827547
A1 20050616 US 2004-500071
                                                                20021225
                        A1
    US 2005130955
                                                                 20040625
    US 7229985 B2 20070612
JP 2001-393016 A 20011226
WO 2002-JP13558 W 20021225
PRAI JP 2001-393016
    Disclosed are amorphous 2-(1-isopropoxycarbonyloxy-2-methylpropyl)-7,8-
    dimethoxy-4(5H),10-dioxo-2H-1,2,3-triazolo[4,5-c][1]
    benzazepine (I), which is improved in absorbability and solubility; and
    a medicinal composition containing the compound Also provided are processes
for
    producing amorphous compound I and for producing a medicinal composition
containing
    the compound An amorphous compound I was dissolved in methylene chloride, and
    mixed with Me cellulose (Metolose SM15) and methanol. The mixture was then
    spray dried to obtain an amorphous powder of the present invention.
RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
             ALL CITATIONS AVAILABLE IN THE RE FORMAT
=> s Ishikura Toyoaki/AU
           29 ISHIKURA TOYOAKI/AU
=> s 110 and benzazepine
         2261 BENZAZEPINE
          774 BENZAZEPINES
         2471 BENZAZEPINE
                 (BENZAZEPINE OR BENZAZEPINES)
            1 L10 AND BENZAZEPINE
L11
=> dis 111 bib abs
L11 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN
AN
    2003:532667 CAPLUS
DN
    139:90493
ΤI
    Amorphous substance of tricyclic triazolobenzazepine derivative
    Ishikura, Toyoaki; Ishizawa, Takayuki; Suemune, Kenji; Ishiwata,
    Mayumi; Udagawa, Chikako
    Meiji Seika Kaisha, Ltd., Japan
PΑ
SO
    PCT Int. Appl., 25 pp.
    CODEN: PIXXD2
DT
    Patent
LA
    Japanese
FAN.CNT 2
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PATENT NO.
                   KIND DATE APPLICATION NO. DATE
    WO 2003055886 A1 20030710 WO 2002-JP13558 20021225
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ,
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                        A1 20030710 CA 2002-2471651 20021225
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A1 20041013 EP 2002-790871
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                                                                   20021225
     EP 1466914
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A1 20050616 US 2004-500071 20040625
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     US 2005130955
    US 7229985 B2 20070612
JP 2001-393016 A 20011226
WO 2002-JP13558 W 20021225
PRAI JP 2001-393016
     Disclosed are amorphous 2-(1-isopropoxycarbonyloxy-2-methylpropyl)-7,8-
     dimethoxy-4(5H),10-dioxo-2H-1,2,3-triazolo[4,5-c][1]benzazepine
     (I), which is improved in absorbability and solubility; and a medicinal
composition
     containing the compound Also provided are processes for producing amorphous
     compound I and for producing a medicinal composition containing the compound
Αn
     amorphous compound I was dissolved in methylene chloride, and mixed with Me
     cellulose (Metolose SM15) and methanol. The mixture was then spray dried to
     obtain an amorphous powder of the present invention.
RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
             ALL CITATIONS AVAILABLE IN THE RE FORMAT
=> s 110 and coprecip?
          6863 COPRECIP?
          2591 COPPT
          1482 COPPTS
          3609 COPPT
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          6440 COPPTD
          1034 COPPTG
         17317 COPPTN
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L12
             2 L10 AND COPRECIP?
=> dis 112 1-2 bib abs
L12 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
ΑN
     2004:1154779 CAPLUS
DN
     142:62766
ΤI
    Product of coprecipitation of sparingly soluble substance and
     water-soluble polymer and process for producing the same
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Ishikura, Toyoaki; Udagawa, Chikako; Misaka, Masato; Suemune,

ΤN

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PΑ
     Meiji Seika Kaisha, Ltd., Japan
SO
     PCT Int. Appl., 31 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     Japanese
FAN.CNT 2
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                        A1 20041229 WO 2004-JP8727 20040621
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            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
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                     A1 20070719
     US 2007167402
                                          US 2005-561212
PRAI JP 2003-175646
                               20030620
                         Α
     WO 2004-JP8727
                               20040621
                         W
     Disclosed is a product of the copptn. of 2-(1-isopropoxy-
AΒ
     carbonyloxy-2-methylpropyl)-7,8-dimethoxy-4(5H),10-dioxo-2H-1,2,3-
     triazolo[4,5-c][1]benzoazepine (I) and a water-soluble polymer. The
     copptn. product is excellent in solubility and absorbability. Crystalline I
     and Me cellulose were dissolved in DMSO. The mixture was dropped into an
     aqueous solution containing Me cellulose to give ppts., which showed a
solubility 16.8
     \mug/mL, as compared to 0.8 \mug/mL for crystalline I.
RE.CNT 15
             THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
             ALL CITATIONS AVAILABLE IN THE RE FORMAT
    ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
     2004:1154759 CAPLUS
ΑN
DN
     142:76996
ΤI
    Manufacture of coprecipitates of water-insoluble substances and
     water-soluble polymers
ΙN
     Chikase, Shigeru; Misaka, Masato; Udagawa, Chikako; Ishikura,
     Toyoaki
    Meiji Seika Kaisha, Ltd., Japan
PA
     PCT Int. Appl., 21 pp.
SO
     CODEN: PIXXD2
DT
     Patent
LA
     Japanese
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    WO 2004113424 A1 20041229
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            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,

Kenji; Kitahara, Shinichi; Ono, Kiyoko; Koyanagi, Akihiro

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             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
                               20030620
PRAI JP 2003-175646
                         Α
    The title coppts. are manufactured by mixing of solns. of the
     water-insol. substances(e.g., medicines) in aqueous organic solvents(e.g.,
DMSO,
     N, N-DMF) into flowing liquid media mainly containing water, and continuous
     flowing for copptn., whereas the solns. and/or liquid media
     contain the water-soluble polymers(e.g., cellulose).
              THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT 2
             ALL CITATIONS AVAILABLE IN THE RE FORMAT
=> s Udagawa Chikako/AU
             4 UDAGAWA CHIKAKO/AU
L13
=> dis 113 1-4 bib abs
L13 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
ΑN
     2004:1154779 CAPLUS
DN
     142:62766
TΙ
     Product of coprecipitation of sparingly soluble substance and
     water-soluble polymer and process for producing the same
     Ishikura, Toyoaki; Udagawa, Chikako; Misaka, Masato; Suemune,
ΙN
     Kenji; Kitahara, Shinichi; Ono, Kiyoko; Koyanagi, Akihiro
PA
    Meiji Seika Kaisha, Ltd., Japan
SO
     PCT Int. Appl., 31 pp.
     CODEN: PIXXD2
DT
    Patent
    Japanese
LA
FAN.CNT 2
     PATENT NO.
                               DATE
                                          APPLICATION NO.
                                                                 DATE
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                                          WO 2004-JP8727
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PΙ
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                        A1
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             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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                         Α1
                               20070719
                                           US 2005-561212
                                                                   20051219
PRAI JP 2003-175646
                         Α
                                20030620
     WO 2004-JP8727
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                               20040621
     Disclosed is a product of the copptn. of 2-(1-isopropoxy-carbonyloxy-2-
     methylpropy1)-7,8-dimethoxy-4(5H),10-dioxo-2H-1,2,3-triazolo[4,5-
     c][1]benzoazepine (I) and a water-soluble polymer. The copptn. product is
     excellent in solubility and absorbability. Crystalline I and Me cellulose were
     dissolved in DMSO. The mixture was dropped into an aqueous solution
containing Me
     cellulose to give ppts., which showed a solubility 16.8 \mug/mL, as compared
     to 0.8 \mug/mL for crystalline I.
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RE.CNT 15
                 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
                 ALL CITATIONS AVAILABLE IN THE RE FORMAT
L13 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
      2004:1154759 CAPLUS
ΑN
      142:76996
DN
ΤI
      Manufacture of coprecipitates of water-insoluble substances and
      water-soluble polymers
IN
      Chikase, Shigeru; Misaka, Masato; Udagawa, Chikako; Ishikura,
      Meiji Seika Kaisha, Ltd., Japan
PA
      PCT Int. Appl., 21 pp.
SO
      CODEN: PIXXD2
DT
      Patent
      Japanese
LA
FAN.CNT 2
                             KIND DATE APPLICATION NO.
      PATENT NO.
                                                                                   DATE
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      WO 2004113424
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                SN, TD, TG
PRAI JP 2003-175646
                                        20030620
                                Α
      The title coppts. are manufactured by mixing of solns. of the water-insol.
      substances(e.g., medicines) in aqueous organic solvents(e.g., DMSO, N,N-DMF)
into
      flowing liquid media mainly containing water, and continuous flowing for
      copptn., whereas the solns. and/or liquid media contain the water-soluble
      polymers(e.g., cellulose).
RE.CNT 2
                 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
                 ALL CITATIONS AVAILABLE IN THE RE FORMAT
     ANSWER 3 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
ΑN
      2003:532667 CAPLUS
DN
      139:90493
TΙ
      Amorphous substance of tricyclic triazolobenzazepine derivative
      Ishikura, Toyoaki; Ishizawa, Takayuki; Suemune, Kenji; Ishiwata, Mayumi;
ΙN
      Udagawa, Chikako
      Meiji Seika Kaisha, Ltd., Japan
PA
      PCT Int. Appl., 25 pp.
SO
      CODEN: PIXXD2
DT
      Patent
LA
      Japanese
FAN.CNT 2
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                                        DATE
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                              A1 20030710
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                GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
                PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
                UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
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                                                                   20021225
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                                                                   20040625
     US 7229985
                         В2
                                20070612
PRAI JP 2001-393016
                         Α
                                20011226
     WO 2002-JP13558
                         W
                               20021225
     Disclosed are amorphous 2-(1-isopropoxycarbonyloxy-2-methylpropyl)-7,8-
AB
     dimethoxy-4(5H),10-dioxo-2H-1,2,3-triazolo[4,5-c][1] benzazepine (I), which
     is improved in absorbability and solubility; and a medicinal composition
containing the
     compound Also provided are processes for producing amorphous compound I and
compound I
     was dissolved in methylene chloride, and mixed with Me cellulose (Metolose
     powder of the present invention.
```

for producing a medicinal composition containing the compound An amorphous

SM15) and methanol. The mixture was then spray dried to obtain an amorphous

THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT 11 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

ΑN 1995:995242 CAPLUS

124:57124 DΝ

ΤI Double-stranded derivative of polyoxyethylene-containing lipid and its preparation

Watanabe, Hiroshi; Taniguchi, Kumi; Udagawa, Chikako; Ando, IN Takashi; Nakabayashi, Satoru

PAMeiji Seika K. K., Japan

SO PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DTPatent

Japanese LΑ

FAN.CNT 1

	PATENT NO.					KIND		DATE			APPLICATION NO.					DATE		
					_													
ΡI	WO 9525764				A1 19950928				WO 1995-JP535					19950323				
		W:	JP,	US														
		RW:	ΑT,	BE,	CH,	DE,	DK,	, ES,	FR,	GB,	GR	R, IE	, IT,	LU,	MC,	ΝL,	PΤ,	SE
	JΡ	3631	755			В2		2005	0323		JΡ	1995	-5245	46		19	99503	323
PRAI	US	S 5786387				A	A 19980728				US 1996-553601					19960125		
	JΡ	1994-52181			A		1994	0323										
	JΡ	? 1994-302165				Α		1994	1206									
	WO	1995	JP5	35		W		1995	0323									

AΒ The title lipid useful as drug delivery system or emulsifier is polyethylene glycol bearing long-chain branching group on 1 end. mixing 100 mg 2-cetyloctadecanoic acid with 39 mg 1,1'-carbonyldiimidazole in 1 mL THF at 70° for 1 h, adding 132 mg $\alpha\text{-hydroxy-}\omega\text{-}$ methylpolyoxyethylene dissolved in 1 mL THF containing catalytic amount of NaOEt, and mixing overnight at 70° gave α -(2cetyloctadecanoyl)- ω -methylpolyoxyethylene.

ΙN Chikase, Shigeru; Misaka, Masato; Udagawa, Chikako; Ishikura, Toyoaki Meiji Seika Kaisha, Ltd., Japan PASO PCT Int. Appl., 21 pp. CODEN: PIXXD2 DT Patent Japanese LA FAN.CNT 2 KIND DATE APPLICATION NO. PATENT NO.

DATE

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                                           _____
                               _____
                        A1 20041229 WO 2004-JP8728
PΙ
    WO 2004113424
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
PRAI JP 2003-175646
                        A
                               20030620
     The title coppts. are manufactured by mixing of solns. of the water-insol.
     substances(e.g., medicines) in aqueous organic solvents(e.g., DMSO, N,N-DMF)
into
     flowing liquid media mainly containing water, and continuous flowing for
     copptn., whereas the solns. and/or liquid media contain the water-soluble
     polymers(e.g., cellulose).
RE.CNT 2
             THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
             ALL CITATIONS AVAILABLE IN THE RE FORMAT
L14 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
     1992:439877 CAPLUS
     117:39877
DΝ
ΤI
     The effect of ME1207, a new oral cephalosporin, on the intestinal
     microflora of beagle dogs
ΑIJ
     Tamura, Atsushi; Ida, Takashi; Saito, Sakiko; Suzuki, Heijiro; Niizato,
     Tetsutaro; Misaka, Masato; Nakayama, Etsuko; Wada, Koichi
     Pharm. Res. Cent., Meiji Seika Kaisha, Ltd., Yokohama, 222, Japan
CS
SO
    Chemotherapy (Tokyo) (1992), 40 (Suppl. 2), 65-74
    CODEN: NKRZAZ; ISSN: 0009-3165
DT
    Journal
    Japanese
LA
AΒ
    ME1207 (pivaloyloxymethyl ester of ME1206) was orally administered to
     beagle dogs at 12 mg/kg/day or 250 mg/kg/day for 14 consecutive days.
     feces of each group were normal during the experiment, and no changes such as
     diarrhea were observed A slight decrease of Enterobacteriaceae and a
     transient decrease of anaerobes were observed in the 12 mg/kg/day group. A
     substantial decrease of Enterobacteriaceae was observed and as a result, the
     main fecal flora was Enterococcus spp. in the 250 mg/kg/day group. The
     detection rate of Clostridium difficile was high in the 12 mg/kg/day
     group. The concentration of ME1206 in the feces was low in the 12 mg/kg/day
     group but high (\geq 1000 \, \mu g/g) in the 250 mg/kg/day group.
     \beta-Lactamase activity in the feces was low. The resistant strains
     were observed in the Enterobacteriaceae but not in the Staphylococcus spp.
     during administration of ME1207.
=> s Suemune Kenji/AU
L15
        15 SUEMUNE KENJI/AU
=> s 115 and coprecipi?
          6856 COPRECIPI?
          2591 COPPT
          1482 COPPTS
          3609 COPPT
                 (COPPT OR COPPTS)
          6440 COPPTD
          1034 COPPTG
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61 COPPTNS
         17339 COPPTN
                 (COPPTN OR COPPTNS)
        25837 COPRECIPI?
                 (COPRECIPI? OR COPPT OR COPPTD OR COPPTG OR COPPTN)
L16
             1 L15 AND COPRECIPI?
=> dis 116 bib abs
L16 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN
    2004:1154779 CAPLUS
DN
    142:62766
ΤI
    Product of coprecipitation of sparingly soluble substance and
    water-soluble polymer and process for producing the same
    Ishikura, Toyoaki; Udagawa, Chikako; Misaka, Masato; Suemune,
ΙN
    Kenji; Kitahara, Shinichi; Ono, Kiyoko; Koyanagi, Akihiro
    Meiji Seika Kaisha, Ltd., Japan
PA
SO
    PCT Int. Appl., 31 pp.
    CODEN: PIXXD2
DT
    Patent
LA
    Japanese
FAN.CNT 2
                               DATE
                                          APPLICATION NO.
    PATENT NO.
                       KIND
                       ____
                               _____
                                           _____
                              20041229
                                                                 20040621
    WO 2004113451
                        A1
                                          WO 2004-JP8727
PΙ
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
            TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
            AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
            EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
            SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
    EP 1650266
                         Α1
                               20060426
                                          EP 2004-746196
                                                                  20040621
           AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
    US 2007167402
                                          US 2005-561212
                        A1
                              20070719
                                                                  20051219
PRAI JP 2003-175646
                         Α
                               20030620
    WO 2004-JP8727
                               20040621
AB
    Disclosed is a product of the copptn. of 2-(1-isopropoxy-
    carbonyloxy-2-methylpropyl)-7,8-dimethoxy-4(5H),10-dioxo-2H-1,2,3-
    triazolo[4,5-c][1]benzoazepine (I) and a water-soluble polymer. The
    copptn. product is excellent in solubility and absorbability. Crystalline I
    and Me cellulose were dissolved in DMSO. The mixture was dropped into an
    aqueous solution containing Me cellulose to give ppts., which showed a
solubility 16.8
    \mug/mL, as compared to 0.8 \mug/mL for crystalline I.
             THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
             ALL CITATIONS AVAILABLE IN THE RE FORMAT
=> s Kitahara Shinichi/AU
           26 KITAHARA SHINICHI/AU
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17317 COPPTN

L17

=> s 117 and coprecip?

6863 COPRECIP? 2591 COPPT

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1482 COPPTS
          3609 COPPT
                 (COPPT OR COPPTS)
          6440 COPPTD
          1034 COPPTG
         17317 COPPTN
            61 COPPTNS
         17339 COPPTN
                 (COPPTN OR COPPTNS)
         25841 COPRECIP?
                 (COPRECIP? OR COPPT OR COPPTD OR COPPTG OR COPPTN)
L18
             1 L17 AND COPRECIP?
=> dis 118 bib abs
L18 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN
     2004:1154779 CAPLUS
ΑN
     142:62766
DN
ΤI
     Product of coprecipitation of sparingly soluble substance and
     water-soluble polymer and process for producing the same
ΙN
     Ishikura, Toyoaki; Udagawa, Chikako; Misaka, Masato; Suemune, Kenji;
     Kitahara, Shinichi; Ono, Kiyoko; Koyanagi, Akihiro
PA
     Meiji Seika Kaisha, Ltd., Japan
SO
     PCT Int. Appl., 31 pp.
     CODEN: PIXXD2
DT
    Patent
LA
    Japanese
FAN.CNT 2
    PATENT NO.
                       KIND DATE
                                                                  DATE
                                          APPLICATION NO.
                        ____
                              20041229
PΙ
    WO 2004113451
                        A1
                                         WO 2004-JP8727
                                                                  20040621
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
     EP 1650266
                         Α1
                              20060426
                                           EP 2004-746196
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
                               20070719
     US 2007167402
                                           US 2005-561212
                                                                   20051219
                        A1
PRAI JP 2003-175646
                         Α
                                20030620
     WO 2004-JP8727
                                20040621
                         W
     Disclosed is a product of the copptn. of 2-(1-isopropoxy-
AB
     carbonyloxy-2-methylpropyl)-7,8-dimethoxy-4(5H),10-dioxo-2H-1,2,3-
     triazolo[4,5-c][1]benzoazepine (I) and a water-soluble polymer. The
     copptn. product is excellent in solubility and absorbability. Crystalline I
     and Me cellulose were dissolved in DMSO. The mixture was dropped into an
     aqueous solution containing Me cellulose to give ppts., which showed a
solubility 16.8
     \mu g/mL , as compared to 0.8 \mu g/mL for crystalline I.
RE.CNT 15
             THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
             ALL CITATIONS AVAILABLE IN THE RE FORMAT
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=> dis 119 1-5 bib abs

- L19 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
- AN 2005:1078892 CAPLUS
- DN 144:104441
- TI Stereoselectivity of the reduced folate carrier in Caco-2 cells
- AU Narawa, Tomoya; Shimizu, Rikako; Takano, Shuhei; Tsuda, Yasuyuki; Ono, Kiyoko; Yamada, Hideo; Itoh, Tomoo
- CS School of Pharmaceutical Sciences, Kitasato University, Tokyo, Japan
- SO Chirality (2005), 17(8), 444-449 CODEN: CHRLEP; ISSN: 0899-0042
- PB Wiley-Liss, Inc.
- DT Journal
- LA English
- Stereoselectivity of the human reduced folate carrier (RFC1) was examined in AΒ Caco-2 cells using methotrexate (L-amethopterin or L-MTX) and its antipode (D-amethopterin or D-MTX) as model substrates. The initial uptake rate of folic acid (FA) was concentration-dependent, with a Km value of approx. 0.6 μM . The Eadie-Hofstee plot of the RFC1-mediated FA uptake revealed a single component for FA uptake into Caco-2 cells, demonstrating that only RFC1 is involved in FA uptake. L-MTX inhibited FA uptake in a competitive manner with a Ki value of approx. 2 μM , similar to the Km value of L-MTX. D-MTX also competitively inhibited FA uptake with a Ki value being approx. 120 μM , indicating that the affinity of D-MTX is .apprx.60-fold less than that of L-MTX. The stereoselectivity of human RFC1 observed in the present study was consistent not only with the stereoselectivity of rabbit RFC1 observed in rabbit intestinal brush border membrane vesicles but also with the reported differences in oral absorption of amethopterin enantiomers in humans.
- RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L19 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
- AN 2004:1154779 CAPLUS
- DN 142:62766
- TI Product of coprecipitation of sparingly soluble substance and water-soluble polymer and process for producing the same
- IN Ishikura, Toyoaki; Udagawa, Chikako; Misaka, Masato; Suemune, Kenji; Kitahara, Shinichi; Ono, Kiyoko; Koyanagi, Akihiro
- PA Meiji Seika Kaisha, Ltd., Japan
- SO PCT Int. Appl., 31 pp.

CODEN: PIXXD2

- DT Patent
- LA Japanese
- FAN.CNT 2

	PATENT NO.					KIND DATE			APPLICATION NO.					DATE				
ΡI	WO 2004113451		A1 20041229		WO 2004-JP8727					20040621								
		W:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	AZ,	BA,	BB,	ВG,	BR,	BW,	BY,	BZ,	CA,	CH,
			CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,
			GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KΖ,	LC,
			LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NΑ,	ΝI,
			NO,	NΖ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,
			ΤJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UΖ,	VC,	VN,	YU,	ZA,	ZM,	ZW
		RW:	BW,	GH,	GM,	KΕ,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	ΑM,
			AΖ,	BY,	KG,	KΖ,	MD,	RU,	ΤJ,	TM,	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,
			EE,	ES,	FΙ,	FR,	GB,	GR,	HU,	ΙE,	ΙΤ,	LU,	MC,	NL,	PL,	PT,	RO,	SE,
			SI,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	$\mathrm{ML}_{m{\prime}}$	MR,	ΝE,
			SN,	TD,	ΤG													

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EP 1650266
                        20060426
                                   EP 2004-746196
                   Α1
                                                            20040621
   R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
       IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
US 2007167402
                   A1
                          20070719
                                     US 2005-561212
                                                            20051219
```

20030620 Α

PRAI JP 2003-175646 WO 2004-JP8727 W 20040621

AB Disclosed is a product of the copptn. of 2-(1-isopropoxy-carbonyloxy-2methylpropy1)-7,8-dimethoxy-4(5H),10-dioxo-2H-1,2,3-triazolo[4,5c][1]benzoazepine (I) and a water-soluble polymer. The copptn. product is excellent in solubility and absorbability. Crystalline I and Me cellulose were dissolved in DMSO. The mixture was dropped into an aqueous solution containing Me

cellulose to give ppts., which showed a solubility 16.8 $\mu g/mL$, as compared to 0.8 μ g/mL for crystalline I.

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

- ANSWER 3 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN L19
- 2001:146120 CAPLUS ΑN
- 134:320497 DΝ
- ΤT Stereoselectivity of the folate transporter in rabbit small intestine: studies with amethopterin enantiomers
- ΑU Itoh, Tomoo; Ono, Kiyoko; Koido, Kei-Ichi; Li, Yin-Hua; Yamada, Hideo
- CS Department of Pharmaceutics, School of Pharmaceutical Sciences, Kitasato University, Tokyo, 108-8641, Japan
- Chirality (2001), 13(3), 164-169SO CODEN: CHRLEP; ISSN: 0899-0042
- PΒ Wiley-Liss, Inc.
- DT Journal
- LA English
- AΒ Stereoselectivity of the folate transporter was examined using rabbit intestinal brush border membrane vesicles (BBMV). Methotrexate (MTX) and the antipode (D-amethopterin) were used as model substrates of the transporter. Folic acid (FA) and MTX were actively taken up into BBMV in the presence of an H+ gradient. Initial uptake of FA and MTX was concentration-dependent with Km values of 1.5 and 1.6 μ M for FA and MTX, resp. FA and MTX mutually inhibited uptake in a competitive manner, with Ki values being similar to the corresponding Km values, demonstrating that FA and MTX share the folate transporter. D-Amethopterin also inhibited FA uptake competitively, with a Ki value approx. 60-fold greater than that of MTX, showing that the affinity of the D-isomer (D-amethopterin) to the folate transporter is much less than that of the L-isomer (MTX). The extent of stereoselectivity observed in the present study is consistent with the previously reported differences in plasma concentration between amethopterin

enantiomers following oral administration in humans.

- RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L19 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
- 1988:610541 CAPLUS ΑN
- DN 109:210541
- process for the preparation of pyruvic acid or its esters from methacrylic ΤI acid or its esters
- Arashiba, Nobumasa; Asano, Shiro; Ono, Kiyoko ΙN
- PAMitsui Toatsu Chemicals, Inc., Japan
- Jpn. Kokai Tokkyo Koho, 5 pp. SO CODEN: JKXXAF
- DTPatent
- LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE		
ΡI	JP 63126840	А	19880530	JP 1986-272807	19861118		
PRAI	JP 1986-272807		19861118				

OS CASREACT 109:210541

AB Pyruvic acid (I) or its esters are prepared by O3-oxidation of methacrylic acid (II) or its esters, followed by hydrogenation of the resulting reaction mixture in the presence of Pd at ≤15°. A solution of II in MeOH was bubbled with O3-containing O between -15 and -20° for 70 min and the reaction mixture was treated with Pd/C with feeding of H between -5 and -10° for 30 min to give 97% I (conversion 100%), vs. 1% (conversion 100%) for a control by hydrogenation at 17-20°.

- L19 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
- AN 1988:437513 CAPLUS
- DN 109:37513
- TI Process for the preparation of glyoxylic acid useful as intermediates for pharmaceuticals and agrochemicals
- IN Arashiba, Nobumasa; Asano, Shiro; Ono, Kiyoko
- PA Mitsui Toatsu Chemicals, Inc., Japan
- SO Jpn. Kokai Tokkyo Koho, 6 pp. CODEN: JKXXAF
- DT Patent
- LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ΡI	JP 62298552	A	19871225	JP 1986-139211	19860617
PRAI	JP 1986-139211		19860617		

OS CASREACT 109:37513

AB Glyoxylic acid (I), a known intermediate for pharmaceuticals, agrochems., cosmetics, and perfumes, is prepared from maleic acid (II) with high selectivity and yield. To II dissolved in MeOH at -45 to -40°, was fed 0.93 volume% O3 in O2 for 2 h followed by N for 15 min and then the reaction mixture was stirred at 10 kg/cm2 H gage in the presence of 52 weight% Pd/Al2O3 to heat slowly up to 10° in 1.5 h and for further 1 h at 10° to give 93% I (II conversion at 100%) without peroxide formation.

=> s Koyanagi Akihiro/AU

L20 7 KOYANAGI AKIHIRO/AU

 \Rightarrow dis 120 1-7 bib abs

L20 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2006:156927 CAPLUS

DN 144:403759

- TI Tricyclic pharmacophore-based molecules as novel integrin $\alpha v\beta 3$ antagonists. Part 2: Synthesis of potent $\alpha v\beta 3/\alpha IIb\beta 3$ dual antagonists
- AU Ishikawa, Minoru; Kubota, Dai; Yamamoto, Mikio; Kuroda, Chizuko; Iguchi, Maki; Koyanagi, Akihiro; Murakami, Shoichi; Ajito, Keiichi
- CS Pharmaceutical Research Department, Meiji Seika Kaisha, Ltd., Yokohama, 222-8567, Japan
- SO Bioorganic & Medicinal Chemistry (2006), 14(7), 2109-2130 CODEN: BMECEP; ISSN: 0968-0896
- PB Elsevier B.V.
- DT Journal
- LA English

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We synthesized 4-aminopiperidine derivs. of our prototype integrin
AΒ
     \alpha v \beta 3 antagonist 1 in an attempt to increase the activity and
     water solubility Introduction of one or two hydrophilic moieties into the
     central aromatic ring and/or the benzene ring at the C-terminus of 1
     increased water solubility and enhanced inhibition of cell adhesion.
                                                                           The
     results of a structure-activity relationships (SAR) study indicated that
     the torsion angle between the central aromatic ring and the piperidine ring,
     and the acidity at the sulfonamide moiety, might be important for
     \alpha v\beta 3 receptor binding activity. Some of these compds. are
     novel and potent \alpha v\beta 3/\alpha IIb\beta 3 dual antagonists with
     acceptable water solubility and a satisfactory early absorption, distribution,
     metabolism, excretion, and toxicity (ADMET) profile.
              THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT 30
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
    ANSWER 2 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
L20
     2004:1154779 CAPLUS
ΑN
     142:62766
DN
     Product of coprecipitation of sparingly soluble substance and
ΤI
     water-soluble polymer and process for producing the same
ΙN
     Ishikura, Toyoaki; Udagawa, Chikako; Misaka, Masato; Suemune, Kenji;
     Kitahara, Shinichi; Ono, Kiyoko; Koyanagi, Akihiro
PA
     Meiji Seika Kaisha, Ltd., Japan
SO
     PCT Int. Appl., 31 pp.
     CODEN: PIXXD2
DT
    Patent
LA
    Japanese
FAN.CNT 2
                       KIND
                                                                  DATE
    PATENT NO.
                               DATE
                                           APPLICATION NO.
                        ----
                               20041229
                                                                   20040621
PΙ
    WO 2004113451
                         A1
                                         WO 2004-JP8727
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
     EP 1650266
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                               20060426
                                           EP 2004-746196
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
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                                20070719
                                           US 2005-561212
     US 2007167402
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PRAI JP 2003-175646
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                                20030620
     WO 2004-JP8727
                                20040621
                          W
     Disclosed is a product of the copptn. of 2-(1-isopropoxy-carbonyloxy-2-
AB
     methylpropy1)-7, 8-dimethoxy-4(5H), 10-dioxo-2H-1, 2, 3-triazolo[4,5-
     c][1]benzoazepine (I) and a water-soluble polymer. The copptn. product is
     excellent in solubility and absorbability. Crystalline I and Me cellulose were
     dissolved in DMSO. The mixture was dropped into an aqueous solution
containing Me
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cellulose to give ppts., which showed a solubility 16.8 μ g/mL, as compared to 0.8 μ g/mL for crystalline I.

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN AN 2001:695818 CAPLUS

- DN 136:363213
- TI Role of transporter and metabolic enzyme in sequential and competitive process of intestinal absorption: Study on SGLT1, disaccharidase and peptidases
- AU Mizuma, Takashi; Matsumoto, Seiichi; Hagi, Katsura; Koyanagi, Akihiro; Narasaka, Takuo; Fuseda, Norihiko; Hayashi, Masahiro; Awazu, Shoji
- CS Department of Biopharmaceutics, School of Pharmacy, Tokyo University of Pharmacy and Life Science, Hachioji, Tokyo, Japan
- SO Yakubutsu Dotai (2001), 16(3), 258-263 CODEN: YADOEL; ISSN: 0916-1139
- PB Nippon Yakubutsu Dotai Gakkai
- DT Journal
- LA Japanese
- We have studied intestinal metabolism and transport, which is considered to be AΒ a sequential (1) or competitive (2) process in absorption (Scheme 1). Disaccharide (maltose, cellobiose, lactose) conjugates of p-nitrophenol were hydrolyzed to p-nitrophenyl β -glucosides (p-NP β glc) on the mucosal side. The p-NP β glc was transported by Na+/glucose cotransporter (SGLT1). Transport clearance of p-NP β glc formed from cellobiose and lactose conjugates of p-NP were higher than that from maltose or of p-NP β qlc itself. These results suggest that SGLT1 is cooperatively coupled with lactase/phloridzin hydrolase catalyzing hydrolysis of cellobiose and lactose conjugates. There might be a cooperative relationship between peptidase and H+/oligopeptide cotransporter or amino acid transporter as well. (2) Kyotorphin (KTP) was too unstable in intestine to be absorbed. KTP appeared on the serosal side in the presence of peptidase inhibitors. Meanwhile, cyclic KTP was stable in intestine to be absorbed. Absorption clearance of cyclic KTP was higher than the overall transport clearance of KTP, which was calculated according to the metabolic inhibition model. Competitive process was observed in intestinal absorption of α -naphthol as well. These results indicate that metabolism degradation and membrane transport are competitive. Unless a drug is stabilized against metabolic enzyme, intestinal absorption of the drug can not be improved even if membrane transport is increased.
- L20 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
- AN 2001:311798 CAPLUS
- DN 135:252146
- TI Critical factor in intestinal absorption of peptide drugs: Quantitative analysis of peptide drug absorption which is competitive process of metabolism and transport
- AU Mizuma, Takashi; Koyanagi, Akihiro; Awazu, Shoji
- CS Department of Biopharmaceutics, Tokyo Yakka University, Tokyo, Japan
- SO Peptide Science (2001), Volume Date 2000, 37th, 259-262 CODEN: PSCIFQ; ISSN: 1344-7661
- PB Japanese Peptide Society
- DT Journal
- LA English
- AB Intestinal absorption of modified kyotorphin (KTP) analogs were kinetically evaluated. Absorption clearance (CLabs) of cyclic KTP, KTP-pAP β glc and Boc-KTP-pAP β glc were higher than that of KTP (0.247 μ l/min/cm) indicating that derivatization of KTP increases the membrane permeability. Furthermore, the greater the metabolic clearance (CLmet) of KTP and its derivs., the lower the CLabs. These results and simulation study led to the conclusion that intestinal absorption of peptide drugs is a competitive process of metabolism and transport and that metabolic degradation in the intestinal tissues is more critical than membrane permeability (transport) for oral delivery of peptide drugs.
- RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L20 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
- AN 1997:191199 CAPLUS
- DN 126:287519
- TI Intestinal transport and metabolism of analgesic dipeptide, kyotorphin: rate-limiting factor in intestinal absorption of peptide as drug
- AU Mizuma, Takashi; Koyanagi, Akihiro; Awazu, Shoji
- CS Department of Biopharmaceutics, School of Pharmacy, Tokyo University of Pharmacy and Life Science, 1432-1 Horinouchi, Hachioji, Tokyo, 192-03, Japan
- SO Biochimica et Biophysica Acta, General Subjects (1997), 1335(1-2), 111-119 CODEN: BBGSB3; ISSN: 0304-4165
- PB Elsevier B.V.
- DT Journal
- LA English
- Intestinal transport and metabolism of kyotorphin (KTP) were studied in rat AΒ everted small intestine. KTP on the mucosal side was metabolized completely within 60 min, and any amts. of KTP were not detected on the serosal side. On the other hand, [D-Arg2]-KTP (D-KTP) was stable on the mucosal side to appear on the serosal side. However, N-t-butoxycarbonyl-KTP (Boc-KTP), which was metabolized on the mucosal side faster than KTP, appeared on the serosal side. In intestinal homogenate, KTP was metabolized, and the metabolic clearance (CLmet) was decreased by peptidase inhibitors, bestatin, o-phenanthrolin and tryptophan hydroxamate. In the presence of these peptidase inhibitors, the absorption clearance (CLabs) of KTP was increased. The less the CLmet of KTP was, the more the CLabs of KTP was. Meanwhile, Boc-KTP in intestinal homogenate was stable even in the absence of peptidase inhibitors. CLabs of Boc-KTP was constant irresp. of the stability on the mucosal side. Kinetic anal. by the metabolic inhibition model indicated that the stabilization of KTP in the intestinal tissue could increase the CLabs up to 0.247 $\mu L/\text{min}$ per cm, which was as much as the CLabs of stable D-KTP. These results led to the conclusion that rate-limiting process in intestinal absorption of KTP is metabolic degradation in intestinal tissue during the absorption.
- L20 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
- AN 1996:417940 CAPLUS
- DN 125:123422
- TI Improvement of intestinal absorption of leucine enkephalin by sugar coupling and peptidase inhibitors
- AU Mizuma, Takashi; Ohta, Kunihiro; Koyanagi, Akihiro; Awazux, Shoji
- CS School of Pharmacy, Tokyo University of Pharmacy and Life Science, Tokyo, 192-03, Japan
- SO Journal of Pharmaceutical Sciences (1996), 85(8), 854-857 CODEN: JPMSAE; ISSN: 0022-3549
- PB American Chemical Society
- DT Journal
- LA English
- AB Peptidase-degradable leucine enkephalin (LE) was coupled with cellobiose or gentiobiose. In the absorption expts., cellobiose-coupled LE (CcpLE) was more stable than LE itself on the mucosal side, and CcpLE appeared on the serosal side. Destyrosyl LE coupled with cellobiose was not formed, indicating that sugar coupling provided LE with aminopeptidase resistance. In the presence of angiotensin-converting enzyme and enkephalinase inhibitors, the stability of CcpLE on the mucosal side was increased, and as a result more was absorbed. Furthermore, the absorption clearance was much higher than the value expected from the mucosal concentration of CcpLE. Similar results were observed in the absorption of gentiobiose-coupled LE.

In the LE absorption experiment, however, LE was not detected on the serosal side even in the presence of these peptidase inhibitors. Improvement of intestinal absorption by sugar coupling and peptidase inhibitors was evaluated kinetically, indicating the exclusive contribution of metabolic degradation of LE through intestinal tissues to the absorption process.

- L20 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
- AN 1988:86086 CAPLUS
- DN 108:86086
- TI Preparation of superconductive specimens in yttrium-barium-copper-oxygen system by coprecipitation method
- AU Koyanagi, Akihiro; Ohta, Joji; Koizumi, Hirokazu; Suzuki, Takayoshi
- CS Inst. Ind. Sci., Univ. Tokyo, Tokyo, 106, Japan
- SO Seisan Kenkyu (1987), 39(11), 454-5 CODEN: SEKEAI; ISSN: 0037-105X
- DT Journal
- LA Japanese
- AB To an aqueous solution containing Cu(NO3)2, Y(NO3)3, and Ba(NO3)2 in the molar ratio
- of Y(III):Ba(II):Cu(II) of 1:2:3 was added an aqueous solution containing K oxalate,

followed by adjustment of the pH to neutral or alkaline, to obtain coppt. of Cu(C2O4), Y2(C2O4)3, and Ba(C2O4). The coppt. was pyrolyzed at 750° and finally sintered at 950° in air for 12 h.

Measurements of the d.c. conductivity of the resulting sintered body showed a transition to supercond. at 91-5% with a narrower transition temperature range and higher critical elec. c.d. as compared with a sintered body made from Y2O3, BaCO3, and CuO powders. The sintered body prepared by the copptn. method was composed of fine $(1-2)-\mu m$ grains.